UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,681	08/18/2003	Orville G. Kolterman	254/057CON	4614

44638 7590 07/08/2005

ARNOLD & PORTER LLP (18528)
555 TWELFTH ST, NW
WASHINGTON, DC 20004

EXAMINER	
CELSA, BENNETT M	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 07/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/643,681	KOLTERMAN ET AL.	
	Examiner	Art Unit	
	Bennett Celsa	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-30 and 38-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-30 and 38-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Applicant's amendment dated 5/10/05 is acknowledged.

a. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Claims

Claims 24-30 and 38-59 are currently pending and under consideration.

Election/Restriction

Applicant's election with traverse of 25,28,29 tri-pro human amylin as the elected species in the correspondence dated 10/29/04 is again acknowledged and was previously made final.

Withdrawn Objection (s) and/or Rejection (s)

Applicant's attempt by Preliminary Amendment adding essential subject matter directed to non-patent publications incorporated by reference has overcome the disclosure objections for improper incorporation and failure to provide claim antecedent basis. However, it is noted that failure by applicant to cure the defective Preliminary Amendment (see new objections below) will necessitate the reinstatement of these two prior specification objections.

Upon further consideration, the indefinite rejection over the term "an amylin" is withdrawn in light of adequate specification definition thereof. Applicant's argument regarding the terms "amylin agonist" (e.g. any compound that achieves an effect of reducing or moderating postprandial plasm glucose)and "amylin agonist analogue" (an "amylin agonist" which is structurally related to the peptide amylin) being broad but not indefinite was found persuasive. Accordingly, the indefinite rejections are hereby withdrawn.

Outstanding Objection (s) and/or Rejection (s)

Claim Rejections - 35 USC § 112

2. Claims 25-30 and 41-59 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (NEW MATTER REJECTION).

The presently claimed invention drawn to amylin agonist analogues (and corresponding use thereof) as defined by the presently claimed invention (e.g. A1-Z as defined and wherein one or more are D-amino acids) are not described in the specification; nor has applicant provided an indication where this subgenus is supported. The specification (e.g. pages 28-31 and 42) fails to provide sufficient support for the presently claimed subgenus and proviso relating thereto (D containing amylin analogues).

Additionally, with regard to newly added claims 56-59, the new proviso (a)-(f) which states that "then one or more of any of A1 to M1 is **not an L-amino** acid and Z is not amino" (emphasis provided) lacks specification support for the scope of amino acids encompassed by this terminology encompassing D-amino acids *and beyond.*

Applicant must provide evidence of how the presently claimed invention is supported or cancel the new matter.

Discussion

Applicant's arguments directed to the above new matter rejection were considered but deemed nonpersuasive for the following reasons.

Applicant argues that the submission of a substitute specification incorporating by reference subject matter submitted in the Preliminary Amendment dated 8/18/03 (the date of filing of the present application) includes support for the claim limitations.

This argument was considered but deemed nonpersuasive since both the Preliminary Amendment (not referred to in the oath) and the attempt to add essential subject matter from non-US documents incorporated by reference was deficient. See new specification objection to the Preliminary amendment recited below.

Accordingly, the above new matter rejection is hereby maintained.

3. Claims 24 and 38-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (Lack of Written Description).

It is first noted that written description is legally distinct from enablement: "Although the two concepts of are entwined, they are distinct and each is evaluated under separate legal criteria. The written description requirement, a question of fact, ensures the that the inventor conveys to others that he or she had possession of the claimed invention; whereas, the enablement requirement, a question of law, ensures that the inventor conveys to others how to make and use

the claimed invention." See 1242 OG 169 (January 30, 2001) citing *University of California v. Eli Lilly & Co.*

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.,* 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

> The present claims are directed to a method of reducing or moderating a postprandial rise in plasma glucose in a mammal comprising administering to said mammal an amylin or an amylin agonist in an amount effect(ive) to reduce or moderate a postprandial rise in plasma glucose (e.g. claim 24).

Accordingly, the presently claimed invention is broadly directed to the therapeutic use of "amylin agonists" including "amylin agonist analogues" in any "mammalian subject".

The specification (e.g. page 22) broadly defines "amylin agonists" as "compounds which mimic the effects of amylin"; and it is noted that no structure limitation appears to limit what constitutes an "amylin agonist". Additionally, the term "amylin agonist analogue" is defined as "derivatives" of an amylin which act as "amylin agonists" by a hypothesized "direct/indirect" interaction with amyln receptors or other

receptors to which amylin itself may interact. No disclosure of particular receptors or specific functions are disclosed.

The pharmacological and pharmacokinetic properties of amylin have not been extensively characterize, and are therefore difficult to predict. For example, although amylin shares considerable sequence homology with CGRP's (and to a lesser degree with insulin, relaxins and IGF) its physiological function appears to be distinct from that of the other peptides. Although some aspects of amylin function are accepted in the art, e.g. inhibition of glycogen syntheses and inhibition of gastric secretion, others are not well understood. Additionally, the receptors to which amylin directly or indirectly interacts with in order to elicit a particular effect as referred to in the amylin agonist definition above is not known and difficult to discover. Further, substrate/receptor binding is unpredictable insofar that minor changes in substrate structure may result in an inactive substrate analogue due to the stereospecific requirements of receptor binding. Thus, the amylin art in general including receptor binding and mechanisms of action in particular is highly unpredictable.

The demonstration of efficacy with respect to peptidic amylin analogue which retain amylin core structure and their abilty to reduce or moderate a postprandial rise in plasma glucose is simply not commensurate in scope as compared to the potential "amylin agonists" (both peptidic and nonpeptidic) which are within the scope of the presently claimed invention.

Accordingly, the specification discloses only limited examples that are neither representative of the claimed genus of amylin agonist compounds, nor is it clear that they represent a substantial portion of the claimed genus.

Discussion

Applicant's arguments directed to the written description rejection above were considered but deemed nonpersuasive for the following reasons. Initially, it is noted that the above rejection was modified to remove its application to "amylin agonist analogues" in light of the Preliminary Amendment; however, this modification of the above rejection will be reconsidered if the Preliminary amendment is ultimately denied entry.

Applicant argues that "representative" exemplification of amylin agonists and amylin agonist analogues and Examples 2-4 regarding assays measuring amylin activity along with other known assays is sufficient to demonstrate possession of "amylin agonists".

The Examiner respectfully disagrees.

The specification definition of amylin agonist" e.g. any compound that achieves an effect of reducing or moderating postprandial plasma glucose broadly encompasses not just peptide amylin analog compounds exemplified in the specification by incorporation by reference but broadly encompasses an infinite number of non-peptide compounds affecting postprandial plasma glucose. Providing examples drawn to peptides which retain amylin core structure (e.g. analogs) and which may bind the same or similar receptors as compared to amylin is not representative of a generic that encompasses non-peptidic compounds which affect postprandial plasma glucose. The ability to screen potential compounds where no compound guidance is given in support of a genus (as is the case presently regarding non-peptides and peptides lacking amylin core structure) does not provide adequate written description. See e.g. Univ. Of

Rochester v G. D. Searle and Co. 249 F. Supp. 2d 216 (W.D.N.Y. 2003) affirmed by the CAFC on February 13, 2004 (03-1304) 69 USPQ2d 1886. .

Accordingly, the above rejection is hereby maintained.

Claim Rejections - 35 USC § 112

1. Claims 24 and 38-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of amylin and specifically disclosed amylin analogues (e.g. specific species of proline containing amylin), the specification does not reasonably provide enablement for the use of amylin agonists which differ from anylin agonist analogues as defined and exemplified in the specification. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use, the invention commensurate in scope with these claims.

There are many factors to consider when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any experimentation is "undue". These factors include, but are not limited to:

a. The breadth of the claims.
b. The nature of the invention
c. The state of the prior art;
d. The level of one of ordinary skill
e. The level of predictability in the art;
f. The amount of direction provided by the inventor;
g. The presence or absence of working examples;
h. The quantity of experimentation necessary needed to make or use the invention based on the disclosure;
See :*In re Wands* USPQ 2d 1400 (CAFC 1988):

(1-2) The breadth of the claims and the nature of the invention:

The present claims are directed to a method of reducing or moderating a postprandial rise in plasma glucose in a mammal comprising administering to said mammal an amylin or

an amylin agonist in an amount effect(ive) to reduce or moderate a postprandial rise in plasma glucose (e.g. claim 24). Claims 38-40 encompass mammalian diabetics (e.g. types I or II).

Accordingly, the presently claimed invention is broadly directed to the therapeutic use of "amylin agonists" including "amylin agonist analogues" in any mammalian "subject". Use of the term "amylin agonist" lacks metes and bounds as to what compounds are encompassed within the scope of the presently claimed invention. The specification on page 22 broadly defines an "amylin agonist" as "compounds which mimic the effects of amylin" without disclosing what effects are encompassed or what degree of mimicry is required in order to fit within the open-ended specification definition. It is noted that no structure limitation appears to limit what constitutes an "amylin agonist", nor is there any defined limits with regard to function which is necessary to recognize an amylin agonist . Accordingly, the skilled artisan could not possibly determine without undue experimentation which amylin or other compound might be effective for the desired purpose.

(3 and 5) *The state of the prior art and the level of predictability in the art:*

The pharmacological and pharmacokinetic properties of amylin have not been extensively characterize, and are therefore difficult to predict. For example, although amylin shares considerable sequence homology with CGRP's (and to a lesser degree with insulin, relaxins and IGF) its physiological function appears to be distinct from that of the other peptides. Although some aspects of amylin function are accepted in the art, e.g. inhibition of glycogen syntheses and inhibition of gastric secretion, others are not

well understood. Additionally, the receptors to which amylin directly or indirectly interacts with in order to elicit a particular effect as referred to in the amylin agonist definition above is not known and difficult to discover. Further, substrate/receptor binding is unpredictable insofar that minor changes in substrate structure may result in an inactive substrate analogue due to the stereospecific requirements of receptor binding. Thus, the amylin art in general including receptor binding and mechanisms of action in particular is highly unpredictable.

(4) *The level of one of ordinary skill in the art:*
The level of skill would be high, most likely at the Ph.D. level

(6-7) *The amount of direction provided by the inventor and the existence of working examples.*

The demonstration of efficacy with respect to a amylin agonist peptide analogues regarding reducing or moderating a postprandial rise in plasma glucose is simply not commensurate in scope as compared to the scope of potential "amylin analogs" (both peptidic and nonpeptidic) which are within the scope of the presently claimed invention.

(8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure:

The lack of guidance in the specification as to other non-amylin analogs and amylin derivatives which would be expected to be effective within the various

thereapeutic claimed regimens, necessarily results in undue experimentation for one of ordinary skill wishing to practice the presently claimed invention.

Discussion

Applicant's arguments directed to the enablement rejection above were considered but deemed nonpersuasive for the following reasons. Initially, it is noted that the above rejection was modified to remove its application to "amylin agonist analogues" in light of the Preliminary Amendment; however, this modification of the above rejection will be reconsidered if the Preliminary amendment is ultimately denied entry.

Applicant argues that "representative" exemplification of amylin agonists and amylin agonist analogues and Examples 2-4 regarding assays measuring amylin activity along with other known assays is sufficient to demonstrate enablement of "amylin agonists".

The Examiner respectfully disagrees.

The specification definition of "amylin agonist" e.g. any compound that achieves an effect of reducing or moderating postprandial plasma glucose, broadly encompasses not just peptide amylin analog compounds (exemplified by amylin peptide compounds incorporatied by reference), but broadly encompasses an infinite number of non-peptide compounds affecting postprandial plasma glucose. Providing examples drawn to peptides which retain amylin core structure (e.g. analogs) and which may bind the same or similar receptors as compared to amylin is not representative of a generic that encompasses non-peptidic compounds or non-amylin peptides which affect postprandial plasma glucose. The ability to screen potential compounds where no compound guidance is given in support of a genus (e.g. as is the case presently

regarding non-peptides and peptides lacking amylin core structure) does not provide adequate written description and/or enablement. See e.g. Univ. Of Rochester v G. D. Searle and Co. 249 F. Supp. 2d 216 (W.D.N.Y. 2003) affirmed by the CAFC on February 13, 2004 (03-1304) 69 USPQ2d 1886.

Applicant's argument of each Wand's factor separately was considered but deemed nonpersuasive for the following reasons.

Initially, it is noted that the above enablement rejection although addressing each Wand's factor separately nevertheless considers the totality of the factors in reaching the ultimate inquiry of nonenablement.

As pointed out in the enablement rejection, the breadth of compounds within the scope of the specification definition of "amylin agonist" is enormous encompassing both peptidic and non-peptidic compounds. In support thereof, the specification exemplifies only amylin agonist analogue compounds which necessarily possess the amylin core structure. Accordingly, contrary to applicant's argument the exemplified species are not representative of the scope of amylin agonist compounds and thus the specification provides inadequate guidance as to what non-amylin compounds to make and what properties (beyond postprandial hypertension) to screen for in order to achieve an amylin agonist. Applicant doesn't challenge unpredictability regarding the correlation of structure and function wherein function is reliant on substrate/receptor binding but merely asserts that such determinations are "well within the level of the skill in the art". Although the skill in the art is high (e.g. PhD level), the specification lacks sufficient guidance as to what non-peptidic compounds; or even peptides which lack amylin core structure; would be deemed to possess amylin agonist activity. One must envision the structure of an amylin agonist

before one is afforded the luxury of performing screening assays. Thus, evaluation of the Wand's factors taken as a whole e.g. the overly broad nature of "amylin agonist" compounds; the unpredictability of the art and the lack of representative examples would necessarily result in undue experimentation regardless of the high level of skill and the availability of assays to such skilled artisans.

Accordingly, the above rejection is hereby maintained.

Claim Rejections - 35 USC § 102/ § 103

2. Claims 24 and 38 are rejected under 35 U.S.C. 102(e) as being anticipated by Liu et al. U.S. Pat. No.6,136,820 (10/2000: filed 12/90 or earlier).

The present claims are directed to a method of reducing or moderating a postprandial rise in plasma glucose in a mammal comprising administering to said mammal an amylin or an amylin agonist (e.g. claim 24). Claim 38 encompass mammalian diabetics (e.g. types I or II). "Amylin agonists" "refers to compounds which mimic the effects of amylin" (original specification page 22, lines 3-5: substitute specification page 13-15) . One amylin effect encompasses the ability of amylin to reduce post-prandial plasma glucose levels" (e.g. see original specification page 21, lines 6-12: substitute specification page 13, lines 4-8).

Liu et al. Discloses and claims treating diabetes (e.g. in mammals) and postprandial hyperglycemia in diabetic individuals (e.g. mammals i.e. humans) by administering castanospermine (e.g. an "amylin agonist"). See specification (e.g. col. Bottom of column 1 to top of col. 2; examples; and patent claims, especially claims 1-2.

Discussion

Applicant's arguments directed to the above anticipation rejection were considered but deemed nonpersuasive for the following reasons.

Applicant argues that "The Examiner appears to conclude that any molecule that treats postprandial hyperglycemia is necessarily an amylin agonist". In this regard applicant argues that compounds such as insulin and castanospermine are not "amylin agonists" since they "reduce or moderate" postprandial hyperglycemia via a different mechanism than amylin.

This argument is not persuasive for several reasons.

First, the specification provides a definition for the term "amylin agonist" which is broad enough to encompass any compound (REGARDLESS OF STRUCTURE OR MECHANISM: emphasis added) that mimic the effects of amylin. Since the reference compounds mimics an amylin effect (reduce/moderate postprandial hyperglycemia) and is structurally a "compound" as required by the specification definition; accordingly, the prior art compound is an amylin agonist within the scope of applicant's broad definition.

Secondly, applicant cannot rewrite the specification definition to include a mechanistic (or structural requirement for that matter) requirement not present in the specification definition. Applicant's arguments in this regard are not commensurate in scope to the claimed invention which incorporates the broad specification definition.

Accordingly, the above anticipation rejection is hereby maintained.

3. Claims 24 and 38-40 are rejected under 35 U.S.C. 102(e) as being anticipated by Liu et al. U.S. Pat. No.6,136,820 (10/2000: filed 12/90 or earlier) or alternatively prima facie obvious in view of Meezan et al. U.S. Pat. No. 5,817,634 (10/98: filed 3/93) for purposes of defining the state of the prior art regarding "diabetes mellitus".

The present claims are directed to a method of reducing or moderating a postprandial rise in plasma glucose in a mammal comprising administering to said mammal an amylin or an amylin agonist (e.g. claim 24). Claim 38 encompass mammalian diabetics comprising diabetes mellitus types I or II (claims 39-40, respectively). "Amylin agonists" "refers to compounds which mimic the effects of amylin" (specification page 22, lines 3-5) . One amylin effect encompasses the ability of amylin to reduce post-prandial plasma glucose levels" (e.g. see specification page 21, lines 6-12).

Liu et al. Discloses and claims treating diabetes (e.g. in mammals) and treating (e.g. reducing or moderating) postprandial hyperglycemia in diabetic individuals (e.g. mammals i.e. humans) by administering castanospermine (e.g. an "amylin agonist"). See specification (e.g. col. bottom of column 1 to top of col. 2; examples; and patent claims, especially claims 1-2.

To the extent that Liu, although disclosing the treatment of diabetes mellitus and claiming the treatment of diabetes, fails to explicitly addresses diabetes mellitus types 1 and 2 the Meezan reference teaching is noted.

Meezan discloses (in its background section: col. 1) that "Diabetes mellitus consists of two (2) subtypes Type I and II both of which are "best characterized by hyperglycemia due to an absolute or relative lack of insulin".

Accordingly, in light of the Liu reference teaching of treating Diabetes mellitus and hyperglycemia, the treatment of Types I or II utilizing the Liu reference method would be immediately envisaged (e.g. anticipated) or in the alternative prima facie obvious to one of ordinary skill in the art at the time of applicant's invention. The rationale that a small reference genus can serve to either anticipate or alternatively render obvious a species contained therein and the raising of a rejection pursuant to 102/103 as done in the present instance is consistent with both sound legal precedent and PTO practice. See e.g. *In re Schaumann*, 572 F.2d 312, 197 USPQ 5 (CCPA 1978); MPEP 2131.02; MPEP 2144.08

Discussion

Applicant's arguments directed to the above obviousness rejection were considered but deemed nonpersuasive for the following reasons.

Applicant argues that neither the Lui nor Meezan referene "disclose, teach or suggest the ability of amylin or amylin agonists to moderate or reduce a postprandial rise in plasma glucose".

This argument was considered but deemed nonpersuasive for the following reasons.

Initially, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

With regard to the Meezan reference it is clear that this reference was cited for its teaching that both types of diabetes (e.g. types 1 and 2) are characterized by hyperglycemia.

Turning to the Lui reference, as discussed in the obviousness rejection above, the Liu reference clearly teaches an "amylin agonist" compound which moderates or reduces a postprandial rise in plasma glucose.

Applicant's attempt to misclassify the Lui reference compound as a non-amylin agonist compound by introducing a mechanism requirement not present in applicant's own specification definition of an "amylin agonist" is simply not persuasive for several reasons.

First, the specification provides a definition for the term "amylin agonist" which is broad enough to encompass any compound (REGARDLESS OF STRUCTURE OR MECHANISM: emphasis added) that mimic the effects of amylin. Since the reference compounds mimics an amylin effect (reduce/moderate postprandial hyperglycemia) and is structurally a "compound" as required by the specification definition the prior art compound is an amylin agonist within the scope of applicant's broad definition.

Secondly, applicant cannot rewrite the specification definition to include a mechanistic (or structural requirement) requirement not present in the definition. Applicant's arguments in this regard are not commensurate in scope to the claimed invention which incorporated the broad specification definition.

Accordingly, the above obviousness rejection is hereby maintained.

Double Patenting

4. Claims 24-30 and 38-59 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-35 (especially claims 32-35) of U.S. Patent No. 6,114,304 .

The present claims are directed to a method of *reducing or moderating* a postprandial rise in plasma glucose *in a mammal* comprising administering to said mammal an amylin or an amylin agonist (e.g. claim 24). Claims 38-40 and 57-59 encompass mammalian diabetics (e.g. types I or II). A preferred (e.g. elected) "amylin analog" is 25,28,29 Pro-h-amylin.

The patent claims are directed to a method of *treating* postprandial hyperglycemia *in a subject*" comprising administering the subject an amount of an amylin agonist of claims 1-12 (including 25,28,29 Pro-h-amylin)

The patent claimed method differs by not expressly teaching:

a. "treating" encompassing "reducing/moderating postprantial hyperglycemia; and

b. "subject" encompassing mammals such as humans.

However, the patent disclosure (e.g. bottom of col. 8) clearly demonstrates that the patented method of treating "inherently" reduces (e.g. moderates) postprandial hyperglycemia (e.g. see col. 8, lines 47-62) which is diabetic induced (e.g. see also col. 6, especially lines 8-21). Additionally, the patent disclosure examples specifically directed to (diabetic) human (e.g. mammalian) subjects (e.g. see Example 2: figures 1-8 clinical data on humans and dogs) and/or the patented preferred embodiment drawn to *human* amylin analogues (e.g. 25,28,29 Pro-h-amylin) would immediately envisage (e.g. anticipate) or alternatively render obvious the

application (e.g. the selection of mammalian subjects) of the patented method to mammalian (diabetic) subjects to one of ordinary skill in the art.

Discussion

In response to the above double patenting rejection, applicant has indicated that a terminal disclaimer will be filed, upon withdrawal of all other outstanding rejections and objections.

Accordingly, the above rejection is hereby maintained.

5. Claims 24-30, 38, 40-57 and 59 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 (especially claims 1-12 and 18) of U.S. Patent No. 6,417,164 .

> The present claims are directed to a method of *reducing or moderating* a postprandial rise in plasma glucose *in a mammal* comprising administering to said mammal an amylin or an amylin agonist (e.g. claim 24). Claims 38, 40, 57 and 59 encompass mammalian diabetics (e.g. type II). A preferred (e.g. elected) "amylin analog" is 25,28,29 Pro-h-amylin.

The patent claims are directed to a method for *reducing postprandial hyperglycemia* in a *non-insulin-taking Type II diabetic subject* comprising administering (single or divided doses) and amount (e.g. @ 0.05-10 micrograms/kg/day) of an amylin agonist, particularly 25,28,29 Pro-h-amylin.

The patented method clearly represents a "species" within the scope of the presently claimed generic insofar that the patented method is directed to a mammalian subject (e.g. a *non-insulin-taking Type II diabetic subject*) within the scope of the presently claimed invention. The

patent claimed method directed to a non-insulin-taking Type II diabetic clearly encompasses human (e.g. mammalian) subjects as illustrated by the patent examples and/or the claimed use of human amylin analogs , particularly 25,28,29 Pro-h-amylin.

Discussion

In response to the above double patenting rejection, applicant has indicated that a terminal disclaimer will be filed, upon withdrawal of all other outstanding rejections and objections.

Accordingly, the above rejection is hereby maintained.

New Objection (s) and/or Rejection (s)

Specification/Claim Objections

4. Claim 24 is rejected to because of the following informalities: line 3: "amount effect" should be --- amount effective ---. Appropriate correction is required.

5. The preliminary amendment filed 8/18/03 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

a. an amendment to include the incorporated material (e.g. see 37 CFR 1.57(b)-(e)) must be accompanied by: a statement that the material being inserted is the material previously incorporated by reference AND that the amendment contains no new matter. The Preliminary Amendment filed 8/18/03 contains neither statement; AND

b. Preliminary Amendments presented on the filing date are NOT part of the original disclosure UNLESS referred to in the first executed oath or declaration. See 37 CFR 1.115 (NOTE: new rule that preliminary amendments present on date of application filing are treated as part of the original disclosure is effective only for applications filed on or after September 21, 2004).

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

6. Claims 24-30 and 38-59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (NEW MATTER REJECTION).

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In amended claim 24 (and claims dependent thereon), the Examiner was unable to locate original specification or original claim support for the phrase " in an amount effect(sic) to **reduce or moderate** ..." nor did applicant indicate where support for the bold language can be found.

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

General information regarding further correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bennett Celsa whose telephone number is 571-272-0807. The examiner can normally be reached on 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bennett Celsa
Primary Examiner
Art Unit 1639

BC
June 30, 2005